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Mowat-Wilson Syndrome

Síndrome de Mowat-Wilson

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As medical specialties, Neurology, Psychiatry, and Clinical Genetics share many affinities, not only because 80% of the human genome is expressed in the central nervous system, but also due to parallels in their history. Congenital abnormalities and traumatic injuries causing neurobehavioral deficits allowed drawing a map of the brain functional structure, beginning in the modern medicine with the notorious report[1] of Phineas Gage casualty in 1848 and the first publication of the cortical cartography represented as a *homunculus* by Penfield and Boldrey[2] in 1937.

In a similar way, translocations and unbalanced abnormalities seen in karyotype of individuals with single gene disorders also allowed locus identification for type 1 neurofibromatosis (17q11.2), Duchenne muscular dystrophy (Xp21), Cornelia de Lange syndrome (5p13.2), and many others. A first map of the human genome was published[3] in 2001 and refined in the following years.

Besides, several chromosomal microdeletion and microduplication present with characteristic neurobehavioral features, such as friendly loquacious personality in Williams syndrome, obsession with eating, food related behavior, and unusual skill with jigsaw puzzle in Prader-Willi syndrome, or polyembolokoilamania, onychotillomania, sleep disturbance, and self-destructive behavior in Smith-Magenis syndrome. The 22q11 deletions in velocardiofacial syndrome are frequently associated with schizophrenia[4]. Patients presenting with these conditions, also denominated contiguous gene disorders, are frequently seen by neurologists, psychiatrists, and clinical geneticists who independently or in interdisciplinary teams helped delineating the neurobehavioral phenotype and consensus diagnostic criteria.

Mowat-Wilson syndrome (MWS) is another example of a condition reflecting these medical specialties overlap. It was initially reported on six children, one of them presenting with a chromosome 2q deletion[5]. In fact, MWS was later associated to heterozygous mutations in the *ZEB2* gene located in 2q22.3 which cause abnormalities in the neural crest development resulting in deviant facial features, functional and structural defects of the central nervous system (development delay, seizures, microcephaly, hypoplasia of the corpus callosum), heart defects, and intestinal aganglionosis leading to Hirschsprung disease[6].

As in most developmental delay syndromes, MWS has been associated to a range of non specific behavioral symptoms like hypotonia, marked delay in the motor milestones, learning problems, moderate to severe intellectual deficiency, epilepsy, attention deficit disorder, and autistic features, but a characteristic neuropsychological profile has also been proposed[6]. Performance in MWS included sociable demeanor and happy affect with frequent laughs, a high rate of oral behaviors (bruxism, chewing or mouthing objects or body parts), an increased rate of repetitive behaviors, under-reaction to pain, and severely impaired or absent speech with contrasting better receptive language[7].

The 15 years following its original description revealed remarkable discoveries regarding MWS physiopathology, molecular basis, inheritance, and phenotypic spectrum, but diagnostic criteria and a precise incidence have not been defined yet. Half of the literature on this condition was published in the last five years and the rate of publications on it increases every year. Thus, the diagnosis of MWS must be considered by professionals that evaluate patients with developmental disorders.

In this issue, Paz et al.[8] present the first series of Brazilian patients diagnosed with MWS, adding new data to the international literature. Seven individuals were diagnosed by mutation analysis of the *ZEB2* gene. Detailed information on dysmorphologic and neurological examination, epileptic history, electroencephalographic findings, Denver II scale evaluation, and brain magnetic resonance imaging are discussed.

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